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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,329	02/15/2006	Gunter Stempfer	BPG33319ASZB	2915

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EXAMINER

NGUYEN, QUANG

ART UNIT	PAPER NUMBER
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1633

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/568,329

Applicant(s)

STEMPFER ET AL.

Examiner

Quang Nguyen, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>7/5/06</u> . | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

Claims 1-22 are pending in the present application, and they are examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 5, it is unclear what is encompassed by the phrase "about 12 hours, about 24 hours or about 48 hours". This is because it is unclear what exactly are the lower and upper limits for a period about 12 hours, about 24 hours and about 48 hours.. The metes and bounds of the claim are not clearly determined. For the purpose of a compact prosecution, the examiner interprets that 36 hours would be about 24 hours or about 48 hours, and the following prior art rejections are applied.

In claim 13, it is unclear what is encompassed by the phrase "for a period of about 12 hours, about 24 hours or about 48 hours at a temperature of about 4 °C, about 10 °C, about 15 °C, about 20 °C or about 25 °C". It is unclear whether Applicants intend to claim the recited time periods and/or temperatures in alternative forms. Should Applicant intend to recite the specific combinations of recited time periods and temperatures, then the term "and" should be inserted between the terms "48 hours" and

“at a temperature” in the above phrase. For the purpose of a compact prosecution, Examiner interprets the claim that all of the recited periods and temperatures are in alternative forms, and therefore the following prior arts are applied. Additionally, the terms “about 24 hours” and “about 48 hours” are unclear because it is unclear what exactly are the lower and upper limits of these recited time periods. Once again, for the purpose of a compact prosecution, the examiner interprets that 36 hours would fall within the scope of about 24 hours or about 48 hours.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 9-14 and 16-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Bochner et al (US 4,680,262; IDS).

Bochner et al discloses a method for the preparation of hGH from transformed *E. coli*, said method comprises culturing a transformant of *E. coli* W3110 tonA, phoA, phoT containing pAP-STII-hGH in 500 mL LB medium and O tetracycline at 37 °C for 8 hrs (please note that during this time period hGH is secreted into the periplasm of the

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transformed *E. coli* host cells and that the transformed cells are concentrated due to growth); followed by seeding the 500 mL inoculum culture into the 10L fermenter containing phosphate-limiting medium at 37 °C and pH 7.5 for 36 hours (about 24 hours or about 48 hours); after which 1-butanol is added to the fermenter and steam is immediately injected into the fermenter jacket so that the temperature of the tank rises rapidly to 50 °C, and it is held at this temperature for 10 minutes (see example 8). Then, the fermenter is rapidly cooled below 20 °C and the cellular contents of the fermenter are harvested by centrifugation. The cell paste, is first frozen at -20 °C and then transferred to -80 °C until further processing is required (col. 5, lines 4-51). Please note any of the steps following fermenting the transformant bacteria in 500 mL culture medium is considered to be an interrupting step prior to extraction.

Accordingly, the teachings of Bochner et al meet every limitation of the instant broadly claims. Therefore, the reference anticipates the instant claims.

Claims 1, 6-8, 13-14 and 16-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Hauptmann et al (US 5,710,027; IDS).

Hauptmann et al discloses a process for preparing IFNalpha, particular human IFNalpha2c, by recombinant expression and secretion of the protein into the periplasmic space in *E. coli* (see at least the Summary of the Invention). Hauptmann et al further teaches a process by exemplification in which prior to the extraction step, the fermentation mixture was cooled down to about 10 °C and at the same time the pH was adjusted to 2.0 using H₂SO₄, and the biomass was separated off by centrifuging and

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stored frozen at -70°C (see example 2, particularly col. 13, lines 61-67). Please also note that prior to the cooling step, the fermentation harvest broth is concentrated due to the growth of the transformed bacteria.

The teachings of Hauptmann et al meet every limitation of the instant claims. Accordingly, the reference anticipates the instant claims.

Claims 1-3, 6-9, 13-14 and 16-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Hart et al (Bio/Technology 12:1113-1117, 1994; IDS).

Hart et al discloses a new method for *in situ* isolation of periplasmic human IGF-I from recombinant *E.Coli*, said method comprises the *in situ* solubilization procedure entailing the steps of adjusting the pH of the fermentation broth to pH10 and the addition of urea and DTT to a respective final concentration of 2M and 10 MM; followed by an incubation at 37°C for about 1 hour, then cooled to 22°C , about 20°C (see at least the abstract and particularly page 1116, right column, first two full paragraphs). The *in situ* solubilization procedure is an interrupting procedure prior to the aqueous two-phase extraction.

The teachings of Hart et al meet all the limitation of the instant claims. Therefore, the reference anticipates the instant claims.

Claims 1, 6-15 and 17-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Kwon et al (US 2004/0151695 A1; IDS).

Kwon et al disclosed a method for producing human interferon alpha, including human interferon alpha b, by recombinantly expressing and secreting the same in the periplasm of a genetically modified *E. coli* (see at least the abstract; paragraph 33 and examples). In an exemplification, Kwon et al teaches that following the induction of IPTG for 3 hours, *E. Coli* transformants were centrifuged at 6,000 rpm for 20 minutes to precipitate the bacterial cells, and the precipitate was suspended in a 1/10 volume of isotonic solution (20% sucrose, 10 mM Tris-HCl buffer containing 1mM EDTA, pH7.0), and the suspension was allowed to stand at room temperature (about 20-25 °C) for 30 minutes, and then centrifuged to collect bacterial cells (example 3). All of these steps are prior to the step of resuspension the collected bacterial cells in D.W. at 4 °C to extract proteins present in the periplasm of the cells; and therefore they constitute the interrupting steps prior to extraction (see example 3, particularly paragraphs 69-70).

Therefore, the teachings of Kwon et al. meet every limitation of the instant claims. Thus, the reference anticipates the instant claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Voitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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QUANG NGUYEN, PH.D.
PRIMARY EXAMINER